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EXAMINER	
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ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,270	SPADAFORA ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,7-9,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *3-5,7-9,12-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 10/22/2009, amended claims 3, 5, 7, 12 and cancelled claims 1-2, 10-11. Applicant's amendment also added new claim 13.

Currently, claims 3-5, 7-9, 12-13 are pending.

Note: Applicant's elect efavirenz as the species in the reply filed on 04/22/2009.

Upon further consideration, the rejection of claims 3-5, 7-9 under 35 U.S.C. 112, first paragraph is herein withdrawn.

Applicant's amendment by deleting the recitation "pharmaceutically acceptable derivatives" overcomes the rejection of claims 3-5, 7-9, and 12 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicant's amendment overcomes the rejection of claims 5, and 12 only as being anticipated by Murdaca et al. The rejection of claims 3-4, 7 under 35 U.S.C. 102(a) as being anticipated by Murdaca et al. (AIDS, 2002, Jan, vol.16, No.2, PTO-1449) is MAINTAINED.

Claims 3-5, 7-9, and 12-13 are examined herein so far as they read on the elected species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 3-4, 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Murdaca et al. (AIDS, 2002, Jan, vol.16, No.2, PTO-1449).

Murdaca et al. discloses a method of treating Kaposi's sarcoma, a cancerous tumor comprising administering to a 37-year old man with KS lesions in the thorax, the face, and the oral cavity, two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, efavirenz. KS lesions are present in the thorax, the face, and the oral cavity i.e epithelial tumors. Murdaca et al. discloses that therapy was well tolerated and led to an increase in the CD4 T cell count, and thoracic-abdominal CT scan proved the absence of nodules in all viscera, confirming complete remission of KS. See the entire article. It is pointed out that administration of efavirenz in treating Kaposi's sarcoma inherently counteracts the loss of cellular differentiation and treats cell proliferation in tumor pathologies such as epithelial tumors, reconverts the differentiated cells into phenotypically normal cells.

Thus, Murdaca et al. anticipate instant claims 3-4, 7.

Response to Arguments

Applicant argues that "The only tumor mentioned in Murdaca is KS. All sarcomas are mesenchymal tumors and not epithelial tumors (i.e., carcinomas)." These arguments have been considered. Murdaca et al. discloses a method of treating Kaposi's sarcoma, a cancerous tumor comprising administering to a 37-year old man with KS lesions in the thorax, the face, and the oral cavity, i.e epithelial tumors, two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse

transcriptase inhibitor, efavirenz. Kaposi's sarcoma is a cancer that causes patches of abnormal tissue to grow under the skin, in the lining of the mouth, nose, and throat or in other organs. It is pointed out that administration of efavirenz in treating Kaposi's sarcoma to a patient with KS lesions in the thorax, the face, and the oral cavity inherently counteracts the loss of cellular differentiation and treats cell proliferation in tumor pathologies such as epithelial tumors.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murdaca et al. as applied to claims 3-4, and 7 above, and in view of Bahal et al. (US 6,235,733, PTO-892).

Murdaca et al. is applied as discussed above.

Murdaca et al. does not explicitly teach the employment of efaviranz in a pharmaceutical composition in the form of pills, suspensions or solutions.

Bahal et al. teaches palatable oral liquid pharmaceutical composition comprising efavirenz in a pharmaceutically acceptable carrier. See abstract ; column 1, lines 63-67; column 3, EXAMPLEs I-IV.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ efaviranz in a pharmaceutical composition in the form solutions for oral administration because Bahal et al. teaches the employment of efavirenz in pharmaceutically acceptable carrier in liquid form for oral administration. One of ordinary skill of art at the time of invention would have been motivated to employ efaviranz in a liquid pharmaceutical composition with carriers with reasonable expectation of employing said pharmaceutical composition for treating Kaposi's sarcoma (tumor).

Response to Arguments

Applicant's arguments have been considered, but not found persuasive as discussed above.

Applicant argues that "the only information that can be gathered from Murdaca is that a regression of KS was observed in association with a triple anti-HIV regimen and a double antibiotic treatment. In fact, there is absolutely no teaching of any effect of efavirenz or any other NNRTI on KS." These arguments have been considered, but not found persuasive. Murdaca et al. discloses a method of treating Kaposi's sarcoma, a cancerous tumor comprising administering two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, efavirenz. Instant claims recite administration of at least one compound selected from nevirapine, efavirenz, and delavirdine. Murdaca discloses administration of efavirenz and thus meets instant claim limitation of at least one compound such as efavirenz.

Applicant argues that "However, Murdaca discloses in its discussion that KS has been reported responding to a combination treatment comprising the same two NRTI (zidovidine and lamivudine) and one protease inhibitor instead of efavirenz (see page 305, first full paragraph). This would have suggested to the person of ordinary skill that if the effect observed in Murdaca is linked to the triple anti-HIV regimen, then it may be attributed to the two nucleoside analog RT inhibitors (zidovidine and lamivudine) rather than to the efavirenz." These arguments have been considered, but not found persuasive as discussed above Murdaca et al. discloses a method of treating Kaposi's sarcoma, a cancerous tumor comprising administering to a 37-year old man with KS lesions in the thorax, the face, and the oral cavity, i.e epithelial tumors two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, efavirenz i.e at least one compound such as efavirenz, and thus meets instant claim limitation. Further, see page 305, right hand top paragraph where Murdaca teaches that HAART regimens with two NRTA and one NNRTI is a choice for the treatment of KS. Accordingly, Murdaca clearly teaches the use of efavirenz in the method of treating Kaposi's sarcoma, a cancerous tumor, and thus meets instant claim limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grimaudo et al. (European Journal of Cancer, vol. 34, pages 1756-1763, 1998, PTO-1449).

Grimaudo et al. teaches a method of treating leukemia comprising administering a non-nucleoside reverse transcriptase inhibitor, thiazolobenzoimidazole derivative (TBZ). See abstract; page 1756, right hand column, line 6-line 10; page 1760, left hand column, paragraph 3. Grimaudo et al. teach that non-nucleoside reverse transcriptase inhibitor TBZ has selective activity on multi drug resistant tumor cells. See page 1762, left-hand, bottom paragraph.

Grimaudo et al. does not teach administration of the particular non-nucleoside reverse transcriptase inhibitor, efavirenz in the method of treating leukemia.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer efavirenz in the method of treating leukemia because Grimaudo et al. teaches that non-nucleoside reverse transcriptase inhibitors are useful in treating leukaemia. One would have been motivated to utilize the specific non-nucleoside reverse transcriptase inhibitors because Grimaudo et al. render the administration of non-nucleoside reverse transcriptase inhibitor to treat leukemia obvious. Accordingly, one would have had an expectation of similar success in treating leukemia with a specific non-nucleoside reverse transcriptase inhibitor, efavirenz, as instantly claimed.

It is pointed out that since Grimaudo et al. renders administration of efavirenz in the method of treating leukemia obvious, administration of efavirenz to leukemia

counteracts the loss of cellular differentiation and treats cell proliferation in tumor pathologies such as epithelial tumors, and reconverts the differentiated cells into phenothypically normal cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, 5, 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ghori et al. (Colorectal Disease, 2000, 2(2), pages 106-112, PTO-1449).

Ghori et al. teaches a method of treating colorectal cancer comprising administering a telomerase inhibitor, a reverse transcriptase inhibitors. Ghori et al. teaches that drugs useful to inhibit RT (exemplified by HIV RT) should effectively inhibit telomerase. Ghori et al. teaches that inhibitors of telomerase could be an effective treatment of cancer, by causing failure of replication of malignant cells. See abstract; pages 106; page 107 left hand parargraph; page 110. Ghori also teaches that tumor cells have higher proliferation rates compared with normal cell populations, which make them more susceptible to anti-telomerase therapy with minimal undesirable effects on normal tissue.

Ghori et al. does not teach administration of the particular telomerase inhibitor, a reverse transcriptase inhibitor, efavirenz in the method of treating colon cancer, glioma, myeloid leukemia.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer efavirenz in the method of treating colon cancer, glioma, myeloid leukemia because 1) Ghori et al. teaches that inhibitors of telomerase could be an effective treatment of cancer, by causing failure of replication of malignant cells, and 2) Ghori et al. teaches that telomerase inhibitors, reverse transcriptase inhibitors are useful in treating colorectal cancer. One would have been motivated to utilize the specific telomerase inhibitor, a reverse transcriptase inhibitor, efavirenz in the method of treating colon cancer, glioma, myeloid leukemia because Ghori et al. render the administration of reverse transcriptase inhibitors to treat cancer obvious. Accordingly, one would have had an expectation of similar success in treating colon cancer, glioma, myeloid leukemia with a specific telomerase inhibitor, reverse transcriptase inhibitor, efavirenz, as instantly claimed.

It is pointed out that since Ghori et al. renders administration of efavirenz in the method of treating colorectal cancer obvious, administration of efavirenz to treat colorectal cancer counteracts the loss of cellular differentiation and treats cell proliferation in tumor pathologies such as epithelial tumors, and reconverts the differentiated cells into phenothypically normal cells.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 7.30 am-3.30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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